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Original article

Validity of bioelectrical impedance analysis in estimation of fat-free mass in colorectal cancer patients

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SUMMARY

Background & aims: Bioelectrical impedance analysis (BIA) is an accessible and cheap method to measure fat-free mass (FFM). However, BIA estimates are subject to uncertainty in patient populations with altered body composition and hydration. The aim of the current study was to validate a whole-body and a segmental BIA device against dual-energy X-ray absorptiometry (DXA) in colorectal cancer (CRC) patients, and to investigate the ability of different empiric equations for BIA to predict DXA FFM (FFM_{DXA}).
Methods: Forty-three non-metastatic CRC patients (aged 50–80 years) were enrolled in this study. Whole-body and segmental BIA FFM estimates ($FFM_{whole\text{-}bodyBIA}$, $FFM_{segmentalBIA}$) were calculated using 14 empiric equations, including the equations from the manufacturers, before comparison to FFM_{DXA} estimates.
Results: Strong linear relationships were observed between FFM_{BIA} and FFM_{DXA} estimates for all equations (R^2 = 0.94–0.98 for both devices). However, there were large discrepancies in FFM estimates depending on the equations used with mean differences in the ranges −6.5–6.8 kg and −11.0–3.4 kg for whole-body and segmental BIA, respectively. For whole-body BIA, 77% of BIA derived FFM estimates were significantly different from FFM_{DXA}, whereas for segmental BIA, 85% were significantly different. For whole-body BIA, the Schols* equation gave the highest agreement with FFM_{DXA} with mean difference ±SD of −0.16 ± 1.94 kg ($p = 0.582$). The manufacturer's equation gave a small overestimation of FFM with 1.46 ± 2.16 kg ($p < 0.001$) with a tendency towards proportional bias ($r = 0.28$, $p = 0.066$). For segmental BIA, the Heitmann* equation gave the highest agreement with FFM_{DXA} (0.17 ± 1.83 kg ($p = 0.546$)). Using the manufacturer's equation, no difference in FFM estimates was observed (−0.34 ± 2.06 kg ($p = 0.292$)), however, a clear proportional bias was detected ($r = 0.69$, $p < 0.001$). Both devices demonstrated acceptable ability to detect low FFM compared to DXA using the optimal equation.
Conclusion: In a population of non-metastatic CRC patients, mostly consisting of Caucasian adults and with a wide range of body composition measures, both the whole-body BIA and segmental BIA device provide FFM estimates that are comparable to FFM_{DXA} on a group level when the appropriate equations are applied. At the individual level (i.e. in clinical practice) BIA may be a valuable tool to identify patients with low FFM as part of a malnutrition diagnosis.

1. Introduction

Rapid loss of fat-free mass (FFM) and skeletal muscle, the major constituent of FFM, has been shown to be an independent predictor of severe toxicity following cancer treatment [1], and to negatively affect efficacy of treatment [2] and survival [3,4]. Depletion of FFM may be masked by a stable body weight or weight gain [5]. In

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cancer patients experiencing treatment-related weight loss, weight gain during or after recovery may be characterized by an increase in fat mass (FM) rather than FFM [6]. Easy available instruments that can be used in the clinic to monitor loss of FFM are therefore needed.

Dual-energy X-ray absorptiometry (DXA) is an instrument that allows for precise whole-body and regional determination of FFM by a low X-ray exposure [7]. Therefore DXA is considered one of the reference methods for measurement of body composition. Access to DXA may, however be limited in clinical practice. Bioelectrical impedance analysis (BIA) is a more easily available method for body composition analysis as it is relatively cheap, provides rapid results and requires minimal operator training. BIA may therefore be a useful tool in clinical practice to identify patients with low FFM as a part of the diagnostic criteria for malnutrition [8]. BIA estimates body composition indirectly. A low-voltage current is passed through the body, whereby impedance (i.e. tissue resistance and reactance) is measured. Impedance data is then utilized in empiric equations to estimate body composition. Such equations have been developed for different populations and incorporate impedance data with variables such as height, weight, age and gender to calculate FFM [9].

There are several types of BIA devices commercially available. Single-frequency BIA measures impedance at one frequency, usually 50 kHz, whereas multi-frequency BIA measures impedance at several frequencies. Moreover, BIA devices can be based on a whole-body or a segmental approach. With the whole-body approach the body is viewed as a cylindrical conductor with a uniform cross-sectional area. This model is demonstrated to be valid in healthy individuals with BMI within the range 16.0–34 kg/m^2, provided that hydration is normal and the BIA equation used is applicable to the population studied [10]. However, since it does not take into account the differences in impedance represented by the various body segments, e.g. the trunk consisting of ~50% of the body weight and only contributing to 5–12% of the whole-body resistance, it has limited validity in populations with abnormal body composition [11]. Segmental BIA has more recently been developed to overcome the inconsistencies between the resistance and body mass of the trunk. Additional research is however required to determine whether this model is better adapted at measuring body composition under these circumstances.

There are a large number of equations available in the literature for estimation of FFM. These equations have mostly been developed in healthy euvolemic adults with a normal body composition. Therefore, the equations may yield less reliable estimates in individuals where these conditions are not met [10]. Patients with colorectal cancer (CRC) are particularly interesting as they are vulnerable to fluid imbalance and alterations in body composition post-operatively and during chemotherapy and/or radiotherapy. CRC patients often experience symptoms such as anorexia, vomiting, diarrhoea and obstipation as a result of treatment. This may adversely affect weight status as well as influence water and electrolyte balance. Furthermore, obesity and abdominal obesity are main risk factors for CRC [12] and thus, many CRC patients will have excess body weight at the time of diagnosis.

Few studies have tested the ability of BIA to estimate FFM in cancer patients using DXA as a reference method, none of which has simultaneously compared two different BIA devices with DXA. Hence, the aim of this study was to validate two different BIA devices, a whole body BIA and a segmental BIA device, against DXA in CRC patients, and to investigate the ability of 14 different empiric equations, including the equations from the manufacturers, to predict DXA FFM (FFM_{DXA}).

2. Methods

2.1. Patients

All patients in this validation study were recruited from an ongoing randomized clinical trial, the Norwegian Dietary Guidelines and Colorectal Cancer Survival (CRC-NORDIET) study. The CRC-NORDIET study is carried out in accordance to the Helsinki Declaration and informed consent was obtained from all participants. The study was approved by the Regional Committees for Medical and Health Research Ethics (REC Protocol Approval 2011/836) and by the data protection officials at Oslo University Hospital and Akershus University Hospital. The study is registered on the National Institutes of Health Clinical Trials (www.ClinicalTrials.gov; Identifier: NCT01570010).

Eligible patients were women and men aged 50–80, with a confirmed CRC (ICD-10 18-20), and staged I-III according to the TNM staging system [13] when they entered the CRC-NORDIET study. Patients with pacemakers were excluded since current from the BIA device could possibly alter the pacemaker activity. To increase generalizability, we chose to include patients with abnormalities in body shape (for example amputations), obesity, orthopedic prosthesis/implants, chronic diseases and fluid disturbances (presence of oedema). All patients had undergone surgery for CRC within the last 4 years.

2.2. Measurements

All measurements took place between December 1st 2015 and February 1st 2016 at the Department of Nutrition, University of Oslo. The patients were instructed to fast overnight and until all measurements were completed. They were also encouraged to void their bladders before measurements. For each patient, all measurements were conducted in the morning in a sequential manner within a timeframe of 2 h.

2.3. BIA

BIA measures body composition indirectly by measuring the impedance of a low-voltage current passing through the body. The impedance consists of two components, resistance (R), the opposition of an ionic solution in both intra- and extracellular spaces and reactance (Xc), representing the capacitance from cell membranes [9]. Estimates of various body compartments, including FFM, are calculated from R or R and Xc values, based on equations, either incorporated in the software or reported in the literature.

Two different BIA devices were used, one whole-body single-frequency (50 KHz) BIA, BIA-101 (SMT Medical, Würzburg, Germany), hereby referred to as whole-body BIA, and a multi-frequency segmental BIA, Seca mBCA515 (Seca, Birmingham, United Kingdom), hereby referred to as segmental BIA. For both instruments, BIA was performed under standardized conditions according to the manufacturer's protocol. All measurements were performed with light clothing and with metal objects (e.g. jewelry, keys) being removed.

The whole-body BIA measurements were performed by placing two adhesive single-use skin electrodes (purchased from Maltron International Ltd, UK) on the right hand and foot, respectively, on the patient when lying in supine position. The device applies a current of 400 μA at constant frequency of 50 kHz.

The segmental BIA measurements were performed on patients standing barefoot on the instrument platform. The device has an integrated scale and uses four pair of electrodes of stainless steel that are positioned at each hand and foot, through which the

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